Remarks

Upon entry of this Amendment, claims 20-25, 27-30, 32-39, 42-58 will be pending. Applicants have amended independent claims 20 and 48, currently on file, to more clearly define the scope of protection being sought. Claims 25, 27, 43, 44 and 56-58 have been amended for consistency. Support for the amendments can be found throughout the specification as filed, for example, at page 6 (lines 14-19), page 13 (line 21) to page 14 (line 1), and in the Examples.

Information Disclosure Statement

The Examiner stated that the information disclosure statement filed June 20, 2007, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited non-patent literature publication or that portion which caused it to be listed. The Examiner stated that the document by Richard Ikegami (1995) has not been considered because the quality of the printed text is not legible. Applicants are submitting herewith a supplemental information disclosure statement together with a more legible copy of the document authored by Richard Ikegami (1995).

35 U.S.C. 112, first paragraph (Written Description)

The Examiner rejected claims 20-25, 27-30, 32-39 and 42-58, under 35 U.S.C. 112, first paragraph, alleging the claims fail to comply with the written description requirement. The Examiner alleged that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner alleged that the specification does not provide an adequate written description for the claimed method of potentiating an immune response comprising administering an antigen covalently attached to a modified PapMV coat protein. The Examiner alleged that, besides discussing general modifications as deletions, insertions, amino acid replacement and like, the specification does not provide further guidance with regard to the modifications that are to be made within the PapMV coat protein in order for the PapMV particle to successfully assemble as a VLP and be used in the method of potentiating an immune response.

In support of this rejection, the Examiner referred to Tremblay *et al.* (FEBS Journal, 2006, Vol 273, p. 14-25; hereinafter referred to as Tremblay) stating that this reference teaches that certain mutations within the capsid protein of PapMV result in failure of PapMV to self assemble into a virus like particle. The Examiner alleged that Applicants do not provide guidance with respect to which mutations, insertions or amino acid replacements within the capsid protein of PapMV would be permissible without risking the failure of the modified PapMV to assemble into a VLP.

Applicants respectfully traverse the Examiner's rejection for the following reasons. Firstly, as stated in MPEP at §2163, "[t]he analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention." [emphasis added]. In this regard, Applicants respectfully remind the Examiner that the claims currently on file are directed to a *method of potentiating an immune response* that comprises administering to an animal an antigen and an effective amount of a specifically defined adjuvant. Applicants assert that, while various plant viruses and plant virus VLPs were known in the art, the immunopotentiating, or adjuvant, properties of such particles had not been previously recognized. The present application, however, clearly describes and demonstrates the ability of a known virus, papaya mosaic virus (PapMV), and VLPs derived from the PapMV coat protein to act as an adjuvant (see, *inter alia*, page 8, paragraph 0039; page 9, paragraph 0044; page 10, paragraph 0047; page 12, paragraph 0055; page 15, paragraph 0068; and the Examples) and the invention as presently claimed relates directly to this newly identified and surprising function of PapMV and PapMV VLPs and to the recognition that assembly of the PapMV coat protein into a specific structure, a VLP, maximizes this adjuvant function (see, for example, page 12, paragraph 0055).

Moreover, MPEP at §2163 clearly indicates that an analysis of whether the specification complies with the written description requirement, "is conducted from the standpoint of one of skill in the art at the time the application was filed (see, e.g., *Wang Labs. v. Toshiba Corp.*, 993 F.2d 858, 865, 26 USPQ2d 1767, 1774 (Fed. Cir. 1993)) and should include a determination of the field of the invention and the level of skill and knowledge in the art. Generally, there is an

inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)" [emphasis added].

As noted by the Examiner in the paragraph bridging pages 3 and 4 of the Office Action, the factors to be considered (in the alternative) in determining whether the specification provides adequate written description of the distinguishing identifying characteristics of a genus include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/functional correlation, methods of making the claimed product, or any combination thereof. In the paragraph that follows on page 4 of the Office Action, however, the Examiner is alleging that only a recitation of structures of the modified coat proteins would provide adequate written description.

Applicants submits that the Examiner's allegation that in the present case, the Applicants have failed to identify the specific distinguishing characteristics of the claimed modified PapMV VLPs, fails to consider: (i) the specification from the standpoint of one skilled in the art with reference to the presently claimed invention relating to a new method of using PapMV and PapMV VLPs, and (ii) the alternative factors to be considered for assessing whether adequate written description has been provided in the specification.

With respect to the claimed method for taking advantage of the first-described recognition of the immunopotentiating properties of a PapMV VLP, the specification describes and illustrates the structure of the VLP itself (see, for example, page 6, paragraph 0027 and Fig. 3) and the function of the VLP as an adjuvant, or immunopotentiator. The instant specification also clearly describes and demonstrates this functional characteristic of immunopotentiation for the PapMV VLPs, as well as for PapMV, and describes the correlation between this functional characteristic and the VLP structure (see, for example, page 9, paragraph 0044; and page 12, paragraph 0055). Also described in the instant specification are methods of making the VLPs from PapMV coat protein (see, for example, page 13, paragraph 0059 to page 14, paragraph 0065; and in the Examples).

The totality of this description is more than enough to convey to one skilled in the art that, at the time the application was filed, Applicants had possession of the claimed invention with regard to the application of both unmodified and modified PapMV VLPs having immunopotentiating properties.

Applicants further note that both the nucleotide sequence encoding the PapMV coat protein and the amino acid sequence of this protein were known in the art at the time of filing (see, AbouHaidar, M.G. *Nucleotide sequence of the capsid protein gene and 3' non-coding region of papaya mosaic virus RNA*, J. Gen. Virol. 69 (PT 1), 219-226 (1988), copy submitted herewith). Moreover, the cloning and generation of various modified PapMV capsid (coat) proteins had been described in the art (see, for example, Lee-Shanok, *Construction and preliminary characterization of papaya mosaic virus as an expression vector for the presentation of foreign epitopes*, Thesis for degree of Master of Science, University of Toronto, 1999; Ikegami, *Papaya mosaic potexvirus as an expression vector for foreign peptides*, Thesis for degree of Master of Science, University of Toronto, 1995; and Sit and AbouHaidar, *Infectious RNA transcripts derived from cloned cDNA of papaya mosaic virus: effect of mutations to the capsid and polymerase proteins,* J. Gen. Virol. 74:1133-1140, 1993, copies submitted with Applicants previous correspondence dated June 20, 2007). In particular, Sit and AbouHaidar describe the generation of a number of recombinant mutant PapMV capsid proteins comprising, for example, amino acid deletions, amino acid insertions, and frame-shift mutations (see, page 1135, 1st column, 2nd and 3rd paragraphs) using techniques that were routine in the art, as evidenced by the description of such techniques in standard texts such as "Molecular Cloning: A Laboratory Manual" (Sambrook *et al.*, 2nd Ed., Cold Spring Habour Laboratory Press, New York, N.Y., 1989) and "Current Protocols in Molecular Biology" (1991, Wiley (NY), F.T. Ausubel, R. Brent, R.E. Kingston, D.D. Moore, J.D. Seideman, J.A. Smith and K. Struhl, eds). In fact, in 2003, when the instant application was filed, protein engineering was a well-established art and the level of skill and knowledge in this art was very high, as evidenced by the large body of literature available in this field at the time of filing. As such, the types of modifications that could be made to a known protein sequence without affecting the function of the protein were well understood by the skilled worker, especially when, as in the present case, the sequences of other similar proteins were available and various mutations to the protein and their effects had

been previously described. In this regard, Applicants submit that the Tremblay reference relied on by the Examiner in effect confirms that the skilled artisan could readily determine from knowledge available in the art, including the sequences of other potexvirus coat proteins, which regions of the PapMV coat protein would be involved in various functions, such as VLP assembly, and which regions therefore would be suitable for modification if this function was to be retained.

As information relating to the genetic modification of proteins, including PapMV coat protein, was available at the time the instant application was filed, Applicants assert that there is no requirement for such information to be described in detail in the present specification. Techniques for confirming the ability of a modified coat protein to assemble into a VLP were also available in the art (see, for example, Lee-Shanok, Ikegami, and Sit and AbouHaidar). In addition, the instant specification provides a clear description of an additional method for testing for assembly of the modified coat protein into a VLP using a system (expression in *E. coli*) well-known in the art (see, for example, Example I and Fig. 2), which does not require that the VLP retain infectivity and is thus simpler to perform than the previously described methods. The instant specification also describes both in words and diagrams the required structure of the VLP (see, for example, page 6, paragraph 0027 and Fig. 3).

As stated in the MPEP at §2163 (Part I) "[T]he essential goal of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject-matter which is claimed. *In re Barker*, 559, F. 2d 588, 592 n. 4, 194 USPQ 470, 473 n. 4 (CCPA 1977). Another objective is to put the public in possession of what the applicant claims as the invention. See *Regents of the University of California v. Eli Lilly,* 119 F 3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997), *cert denied*, 523 U.S. 1089 (1998)." Applicants assert that the description and demonstration provided in the present application of the adjuvant function of PapMV VLPs and the description of the correlation of this function with the VLP structure, together with the description of how to make the VLPs and test for the VLP structure, clearly indicate that Applicants had invented and were in possession of the claimed subject matter. Moreover, this description of the claimed subject-matter, in conjunction with the general knowledge of the PapMV coat protein sequence and methods of genetically modifying proteins available in the art

at the time the instant application was filed, also clearly puts the public in possession of the claimed invention. As such, Applicants assert that claims 20-25, 27-30, 32-39, and 42-58, currently on file, meet the written description requirement as set forth in 35 U.S.C. 112, first paragraph.

Solely for the purpose of expediting the prosecution of the instant application, Applicants have amended the claim set to more clearly define the subject matter for which protection is being sought. In particular, Applicants have amended independent claims 20 and 48 to recite a virus-like particle (VLP) comprising PapMV coat protein or genetically modified PapMV coat protein, and to specify that the PapMV coat protein or genetically modified PapMV coat protein is capable of assembling to form said VLP. Applicants have further amended independent claims 20 and 48 to recite that the genetically modified coat protein comprises one or more amino acid deletions, insertions and/or substitutions. Support for these claim amendments can be found throughout the specification as filed, for example, at page 6 (lines 14-19), page 13 (line 21) to page 14 (line 1), and in the Examples.

Applicants submit that the amended claim set submitted herewith complies with 35 U.S.C. 112, first paragraph, and, therefore, respectfully requests that this rejection be withdrawn.

Conclusion

Applicants submit that all of the stated grounds for rejection have been properly traversed, accommodated or rendered moot. Applicants, therefore, respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided. Prompt and favourable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,
JUNEAU PARTNERS, PLLC

Todd L. Juneau Reg. No. 40,669
JUNEAU PARTNERS, PLLC Customer No. 50438
2121 Eisenhower Avenue, Suite 200
Alexandria, VA 22314
Tel: (703) 548-3569